

REMARKS:

Claim 55 is amended. Claims 55-71 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. §102:

Claims 55-56 and 60-71 stand rejected under 35 U.S.C. §102(e) as being anticipated by Milton (U.S. Patent No. 6,110,669). The Applicant respectfully traverses this rejection.

Claim 55, as amended, is as follows:

A device comprising a plurality of unmodified biopolymer and a solid support, wherein the solid support has at least one surface comprising pendant acyl fluoride functionalities, and wherein an unmodified end of the biopolymer is attached to the solid support by reaction with the pendant acyl fluoride functionalities, in the absence of a spacer arm.

Applicant respectfully submits that Milton cannot anticipate claim 55, because Milton fails to teach a "device comprising a plurality of unmodified biopolymer ... wherein an unmodified end of the biopolymer is attached to the solid support by reaction with the pendant acyl fluoride functionalities, in the absence of a spacer arm." Claim 55 was amended to clarify that an unmodified biopolymer is attached to the solid support in the absence of a spacer arm. It is an unexpected discovery of the present invention that by bringing acyl fluoride functionalities of the solid support into contact with the unmodified biopolymers, biopolymers become efficiently attached to the solid support in the absence of a spacer arm. As emphasized on page 2, lines 20-24, of the specification, such an "efficient attachment" does not require any modifications to either biopolymers, e.g.,

aminating, or fluoride-activated supports, *e.g.*, attachment of spacer arms or linkers. Consequently, the present invention provides a number of advantages over the conventional methods. The advantages include, for example, a simplification of the production of biopolymer arrays and a decrease in their manufacturing costs (page 4, lines 1-8).

The Examiner states that,

“Milton teaches that ‘any protein or peptide with surface amino groups, *e.g.* lysine can be immobilized to a solid support having pendant acyl fluoride functionalities...’ (see column 12, lines 5-7). Thus, Milton discloses that a derivatized protein or peptide is not necessary, since any protein or peptide with surface amino groups, *e.g.* lysine can be immobilized to a solid support having pendant acyl fluoride functionalities.”

The Applicant respectfully disagrees. The quoted statement is a mere speculation, which is not enabled by the disclosure of Milton alone or taken in view of the state of the art at the time the statement was made. Milton does not provide any working examples demonstrating the feasibility of such an attachment. While Milton provides ten working examples demonstrating the attachment of amino-modified and amide-linked biopolymers, Milton does not present any data on the attachment of unmodified biopolymers to acyl fluoride-modified supports. In fact, although Milton proposes attachment through surface amino groups (lysine residues), the illustration that follows immediately after the statement shows attachment only via terminal amine or terminal amide group.

Prior to the present invention, it was generally understood in the art that the attachment of proteins via available terminal amino groups may lead to inefficient and unstable attachment or to reduced activity of the attached biomolecule. For example, as shown in the illustration in columns 11-12 of Milton, attachment via a

terminal group requires a particular orientation of the protein in relation to the acyl fluoride groups of the support. Since biopolymers contact supports in a random orientation, the terminal attachment of biopolymers may suffer from low stability and efficiency.

Because of the possible low attachment efficiency and reduction in biomolecule activity of terminal attachments via naturally present amino groups, this methodology has been abandoned years ago in favor of using post-modified or derivatized biomolecules, which is exactly the approach undertaken by Milton. Milton describes in great detail the attachment of "suitably derivatized biopolymers" on polymeric materials having an acyl fluoride functionality (e.g., column 9, line 63-column 10, line 4; Examples 1, 3, 5, and 6). Milton also teaches the immobilization of biopolymers on solid supports via an amide-linked linker compound (columns 13-14, Examples 7-9). Therefore, in view of the state of the art before the present invention and in the absence of a working example that demonstrates the attachment of unmodified proteins to acyl fluoride supports, the statement quoted by the Examiner does not appear to be enabled by the description provided in Milton.

In summary, Milton does not anticipate instant claim 55 because Milton does not teach the attachment of unmodified biopolymers in general. In particular, Milton does not anticipate instant claim 55 with respect to proteins because the statement provided in column 12 is a mere speculation, which is not enabled by the disclosure of the Milton patent.

Milton cannot make instant claim 55 obvious. In view of the state of the art discussed above, prior to the present invention, one skilled in the art could not have predicted with certainty that biopolymers, including proteins, could be efficiently immobilized directly on substrates without modification and without the use of linkers. This invention unexpectedly demonstrates that such attachment is

possible. Because this result is unexpected, Milton does not make the present invention obvious,

In light of the foregoing, Applicant respectfully submits that Milton could not have anticipated or rendered obvious claim 55, because Milton fails to teach or suggest each and every claim limitation. Claims 56-71 depend from claim 55 and cannot be anticipated or rendered obvious for at least the same reasons as claim 55. Withdrawal of these rejections is thus respectfully requested.

Claims 55-61 and 63-71 stand rejected under 35 U.S.C. §102(e) as being anticipated by Obremski et al. (U.S. Patent No. 6,110,749). The Applicant respectfully traverses this rejection.

Applicant respectfully submits that Obremski cannot anticipate claim 55, because Obremski, similar to Milton fails to teach a “device comprising a plurality of unmodified biopolymer ... wherein an unmodified end of the biopolymer is attached to the solid support by reaction with the pendant acyl fluoride functionalities, in the absence of a spacer arm.” Obremski states, “A short sequence oligonucleotide complementary to the target analyte was covalently coupled to the waveguide using acyl fluoride coupling, and served as the probe.” (Obremski, column 16, line 65-column 17, line 1). This statement is both vague and non-enabling; since it is not even clear from this statement whether the waveguide or the oligonucleotide has an acyl fluoride functionality. In addition, Obremski is silent as to whether the oligonucleotide is modified at the end where the covalent coupling takes place. Thus, in the absence of data to the contrary, a person of ordinary skill in the art would assume that a modification of the oligonucleotide (e.g., 5’amino-modification) took place before the covalent attachment was performed, since this is in keeping with the prior art before the present invention. (Applicant’s specification, at page 1, lines 23-30).

Obremski cannot make instant claim 55 obvious. Obremski has no teaching or suggestion whatsoever of attaching an unmodified end of a biopolymer directly to the acyl fluoride functional groups of a solid support. Furthermore, as discussed above, it is not even clear from Obremski whether it is the solid support which has the acyl fluoride functional groups. Consequently, Obremski doesn't offer the advantages of the present invention discussed above.

In light of the foregoing, Applicant respectfully submits that Obremski could not have anticipated or rendered obvious claim 55, because Obremski fails to teach or suggest each and every claim limitation. Claims 56-61 and 63-71 depend from claim 55 and cannot be anticipated or rendered obvious for at least the same reasons as claim 55. Withdrawal of these rejections is thus respectfully requested.

Applicant believes the foregoing amendments comply with requirements of form and thus may be admitted under 37 C.F.R. § 1.116(a). In addition, admission is requested under 37 C.F.R. § 1.116(a) as presenting rejected claims in better form for consideration on appeal.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6700 to discuss the steps necessary for placing the application in condition for allowance.

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If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

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By



Wei-Ning Yang
Registration No. 38,690
Attorney for Applicants

500 South Grand Avenue, Suite 1900
Los Angeles, California 90071
Telephone: 213-337-6700
Facsimile: 213-337-6701